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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,045	01/19/2005	Masashi Okamoto	10873.1576USWO	4002

52835 7590 05/14/2008

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EXAMINER	
SHAW, AMANDA MARIE	
ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
05/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,045	OKAMOTO ET AL.	
	Examiner	Art Unit	
	AMANDA SHAW	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-12 and 14-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-12 and 14-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 19, 2008 has been entered.

Claims 1, 4-12, and 14-26 are currently pending. Claim 1 has been amended. Claim 26 is newly presented.

Withdrawn Rejections

2. The rejections made under 35 USC 103(a) in sections 4-6 of the Office Action of September 19, 2007 are withdrawn in view of amendments made to the claims. Specifically the claims were amended to recite "centrifuging the centrifugation tube so that the collecting solution containing the microorganism or cell separates from the water absorbing resin particles by passing through the filter and accumulates at the bottom of the centrifugation tube". However a new rejection has been set forth below.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 4, 6-8, 10, 14, 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sato (US 2001/0009759) in view of Lyman (US Patent 4683058 Issued 1987) and Tsuchiya (US Patent 57472747 Issued 1998).

Regarding Claim 1 Sato teaches a method of collecting a virus from a liquid sample using particles capable of being bound by viruses (Abstract). Sato teaches a method of bringing a liquid sample into contact with the particles which in one embodiment are hydrogel particles which absorb water (para 0074). Thus Sato teaches contacting liquid sample with water absorbing particles so that the liquid phase of the sample is absorbed by the water absorbing particles. Sato further teaches that the viruses are caught on the surface of the particles (para 0098). Thus Sato teaches that the viruses are caught on the surface of the water absorbing particles. Sato additionally

teaches pouring a salt solution on the virus bound particles in order to disassociate viruses from the bound particles (para 0099). Thus Sato teaches contacting the water absorbing particles with a collecting solution so as to collect the microorganisms caught on the surface of the water absorbing particles.

Sato does not teach a method wherein the binding of the virus to the particles occurs on a planar filter supported so as to divide the centrifugation tube into an upper space and a lower space. Further Sato does not teach a method wherein during the centrifugation step the microorganisms accumulate at the bottom of the centrifugation tube.

However Lyman teaches a filter for a centrifuge tube. Specifically Lyman teaches a filter tube that is adapted to fit within the upper portion of a standard plastic centrifugation tube. The filter tube has a pressure filter at its lower end and an opening at its upper end for receiving liquids. When the filter tube is filled with a liquid sample comprising permeable and non permeable materials and the composite centrifuge tube and filter tube is spun in the centrifuge, the centrifugal force causes the permeable materials to flow through the filter and collect in the bottom of the centrifuge tube while the non permeable materials are retained in the filter tube (abstract). Thus Lyman teaches pouring a liquid sample into a centrifugation tube and centrifuging the sample so that permeable materials pass through the filter and accumulate at the bottom of the centrifugation tube. Additionally Lyman teaches the filter is made out of polycarbonate (col 4, line 8).

Tsuchiya provides guidance on properly choosing a filter with an appropriate pore size for detecting a particular microorganism (Column 3, lines 45-60). For example Tsuchiya teaches that in order to trap a small bacteria on a filter one could use a filter with a pore size of 0.2μm. Therefore if you wanted that small bacteria to pass through the filter one could use a filter with a pore size larger than 0.2 μm.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention to have modified the method of Sato by performing the step of binding the virus to the particles on a filter in a centrifuge tube and then centrifuging the tube so that the virus accumulates at the bottom of the centrifugation tube as suggested by Lyman and Tsuchiya. In the method of Sato after the salt solution is added, which makes the virus disassociate from the particles, one would be motivated to pass the salt solution and virus particles through a filter located in a centrifuge tube in order to collect the virus. Lyman teaches a composite filter tube and centrifuge tube that allows both separation by filtration through the tube into non permeable materials retained within filter tube and permeable materials collected in the centrifugation tube, and then the further separation of the permeable materials by specific gravity in the centrifuge tube (Column 4, lines 41-47). By placing a filter with the appropriate pore size based on the guidance provided by Tsuchiya in the centrifugation tube of Lyman one can control what size particles or microorganisms are considered permeable. Thus all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions,

and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Regarding Claim 4 Sato teaches a method wherein centrifugation is performed at 15000 rpm for 10 min (para 0141).

Regarding Claim 6 Sato does not teach a method wherein the amount of the collecting solution that is used is greater than the water absorbing capacity of the water absorbing particles. However, it would have been obvious to one of ordinary skill in the art at the time the invention to use an amount of collecting solution that is greater than the capacity of the water absorbing particles so that the collecting solution can elute the virus instead of being absorbed by the particles.

Regarding Claim 7 Sato teaches that the hydrogel particles comprise a sulfonic acid monomer and water-soluble cross-linkable monomer (Para 0074). Thus Sato teaches a method wherein the water absorbing particles are hydrophilic cross-linked polymers having a hydrophilic function group.

Regarding Claim 8 Sato teaches a method wherein the microorganism to be detected is hepatitis B virus (para 0140-0142).

Regarding Claim 10 Sato teaches a method wherein the samples are derived from plasma, serum, cell lysate, urea, saliva and the like (para 0096).

Regarding Claim 14 Sato teaches a method further comprising extracting the viral nucleic acids and then amplifying the nucleic acids (para 0099-0102).

Regarding Claim 25 Sato teaches the nucleic acids are analyzed by PCR (para 0140-0142).

5. Claims 5 and 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sato (US 2001/0009759) in view of Lyman (US Patent 4683058 Issued 1987) and Tsuchiya (US Patent 57472747 Issued 1998) as applied to claim 1 above and in further view of Wardlaw (US Patent 2001/0033808).

The teachings of Sato, Lyman, and Tsuchiya are presented above.

The combined references do not teach a method wherein (i) the amount of the liquid sample added is not greater than a water absorbing capacity of the water absorbing resin (ii) the amount of the liquid sample is in a range from 50 µl to 500 µl or (iiI) the amount of the liquid sample is in a range from 50 mL to 200 mL.

However Wardlaw teaches hydrogels for collecting microorganisms. Wardlaw teaches that the amount of hydrogel required to collect microorganisms from a liquid sample is dependent on the amount of the liquid in the sample. Wardlaw further teaches that it is typically desired to use enough hydrogel so that essentially all of the water in the sample will be absorbed (Para 0011).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Sato, Lyman, and Tsuchiya by using enough hydrogel particles to absorb essentially all of the liquid in the sample as suggested by Wardlaw (Para 0011). Using hydrogel particles capable of absorbing essentially all of the liquid in the sample would aid in the separation and

purification of the virus from the sample. Further it would have been obvious to optimize the volume of the sample used to the amount of hydrogel or vice versa to achieve the best recovery of the microorganism.

6. Claims 9 and 16-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sato (US 2001/0009759) in view of Lyman (US Patent 4683058 Issued 1987) and Tsuchiya (US Patent 57472747 Issued 1998) as applied to claims 1, 8, and 14 above and in further view of Britschgi et al (US Patent 5726021 Issued 10-1998).

The teachings of Sato, Lyman and Tsuchiya are presented above.

Regarding Claim 9 the combined references not teach a method used to collect M. tuberculosis.

However Britschgi et al teach a method of detecting and characterizing different species of Mycobacterium such as M. tuberculosis (Column 6, lines 11-26). Britschgi teaches that the Mycobacterium are present either in a cell culture or from a clinical sample (Column 6, lines 27-28). Further Britschgi teach that the cells can be concentrated prior to lysis by centrifugation and filtration means (Column 7 lines 15-17). After lysis the cellular nucleic acid is extracted and amplified (Columns 8 and 9).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the method of Sato, Lyman and Tsuchiya for isolating M. tuberculosis from cultures before carrying out the nucleic acid extraction and amplification methods of Britschgi (Columns 8-9). An artisan would have been

motivated to include the centrifugation step taught by Sato, Lyman and Tsuchiya in the method of Britschgi because such a step would have allowed for the removal of the cell culture media, cellular debris and other contaminants in the sample which could interfere with the nucleic acid analysis.

Regarding Claims 16-19, 21-22, and 24 the combined references do not teach a method further comprising (i) heating the sample to between 70 ºC and 100ºC; (ii) heating the sample for 1 to 30 min; (iii) heating the sample for 96ºC for 10 min; (iv) using a extraction reagent with a pH between 7-12; (v) using a non ionic detergent; (vi) and using a metal chelating agent.

However Britschgi teaches a method for rapid and sensitive detection of Mycobacterium. The method comprises lysing the mycobacterium cells, extracting the nucleic acid from the lysed cells, and amplifying the lysed cells. Specifically Britschgi et al teach that cell lysis is completed by adding to the cell suspension a lysis reagent that contains a nonionic detergent (e.g. triton X which is a polyoxyethyleneglycol p-t-octylphenyl ether), and incubating the suspension at high temperatures. Britschgi et al further teach that the lysis solution typically has a pH between 6.5 and 10.5. The lysis buffer also preferably contains a chelating agent such as EDTA or EGTA. The cells are incubated in the lysis solution between 75ºC-99ºC until suitable lysis is observed. Typically incubation take 5 minutes or longer at 85ºC. Following lysis the nucleic acids are further analyzed via PCR (Columns 8-9).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Sato, Lyman and Tsuchiya

by examining the cellular constituents by performing nucleic acid analysis as suggested by Britschgi. Using nucleic acid analysis as a method to further examine cells collected from bodily fluids was routinely used in the art at the time of the invention as demonstrated by Britschgi et al and thus it would have been obvious to an ordinary artisan to have examined the collected cells using nucleic acid analysis.

Regarding Claims 20 and 23 the combined references do not teach (i) a method wherein the concentration of the nonionic detergent in the extraction reagent solution is in a range from 0.01 to 10 wt %; or (ii) a method wherein the concentration of the metal chelating agent in the extraction reagent solution is 0.1 to 100 mM.

However, determining the optimum conditions for performing nucleic acid lysis would have been obvious to one of ordinary skill in the art and well within the skill of the art. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller,* 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955).

MPEP 2144.05(b):
"Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)"

"A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)."

7. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sato (US 2001/0009759) in view of Lyman (US Patent 4683058 Issued 1987) and Tsuchiya

(US Patent 57472747 Issued 1998) as applied to claim 14 above and in further view of Krupey (US Patent 5658779 Issued 8/1997).

The teachings of Sato, Lyman, and Tsuchiya are presented above.

The combined references do not teach a method wherein the elution solution is also the lysis solution.

However Krupey teaches a method wherein virus particles are captured on water insoluble particles. Krupey further teaches that the viruses may be desorbed from the particles using extraction agents (Column 12, line 45-47).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Sato, Lyman, and Tsuchiya by using one solution to elute and lysis the virus as suggested by Krupey. Using solutions capable of eluting and lysing viruses at the same time are beneficial because they save time by allowing the eluting and lysing steps to be performed simultaneously thus it would have been obvious to an ordinary artisan to have used such a solution in situations where it was desirable to collect a virus and used the virus for nucleic acid analysis.

Response To Arguments

8. Regarding the response filed February 19, 2007, all of the Applicants arguments pertain to rejections that have been withdrawn. Therefore these arguments are considered moot.

Conclusion

9. No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634

/Ram R. Shukla/

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